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Original Research Article

Methods of induction of labor in intrauterine fetal demise: a comparative study

Saurav Maheshwari*, Deepa Borgohain

Department of Obstetrics and Gynecology, Assam Medical College and Hospital, Assam, India

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***Correspondence:**
Dr. Saurav Maheshwari,
E-mail: drsaurav56@gmail.com

ABSTRACT

Background: This study was undertaken to evaluate and compare the efficacies of two different regimen for induction of labour in IUFD in an effort to find a better management of woman with IUFD.
Methods: It was a hospital based prospective comparative study taken up in the Department of Obstetrics and Gynaecology, Assam Medical College and Hospital (AMCH), Dibrugarh for a period of 1 year. A total number of 90 cases were selected and randomly divided into 2 groups. The two groups were induced using regimen recommended by the RCOG. Group A was induced with Mifepristone - Misoprostol Combined Regimen while Group B was induced with only Misoprostol.
Results: Both the groups were found to be comparable with respect to mean Pre – induction Bishops score. The mean Induction to Onset of Labour Interval and Induction to Delivery Interval were significantly less in Group A as compared to Group B. Mean dose of Misoprostol required was less in Group A compared to Group B. In terms of side effects tolerance to Group A was better than Group B.
Conclusions: It was observed in the study that both the regimen were equally safe, easy to administer and affordable but the Combination Regimen had a slight edge over misoprostol alone regimen in terms of tolerance, fewer side effects and efficacy with regard to early onset of labour, shorter Induction to Delivery Interval and relatively less dose of misoprostol than misoprostol alone regimen.

Keywords: IUFD, Mifepristone, Misoprostol, Oxytocin

INTRODUCTION

The loss of a wanted baby at any gestation is distressing, not only to the expectant parents but also to their relatives and the attending obstetrician.

Despite advances in medical science, diagnostic and therapeutic modalities, pregnancy wastage still occurs, at an unacceptably high rate. Out of the global estimate of 2.6 million stillbirths in 2015 with a Still Birth Rate (SBR) of 18·4 per 1000 births, the majority occurred in the developing countries and India accounted for the highest number of stillbirths.[1]

The terms fetal death, fetal demise, stillbirth, and stillborn all refer to the delivery of a fetus with no signs of life.[2] In 2004 WHO defined Intra Uterine Fetal Demise as death prior to complete expulsion or extraction of a product of human conception from its mother, irrespective of duration of pregnancy and which is not an induced termination of pregnancy.[3] but for international comparison WHO has now recommended IUFD as a baby born with no signs of life at or after 28 weeks' gestation.[4]

When a baby dies in utero, the options are either to wait for labour to start spontaneously or to induce it.[5] Overall,

80-90% of patients enter spontaneous labor within 2 weeks of fetal death.[6-8] In cases where expectant management is chosen, apart from the psychological distress of the mother, the clinical concern would be the development of disseminated intravascular coagulation with its inherent risks of haemorrhage and other complications like infection, septicemia, maternal mortality etc. Therefore, the need arises for induction of labour.

The ideal drug for the termination of pregnancy in cases of IUFD should not only be effective and safe, but should also be affordable to avoid additional financial burden arising from a wasted pregnancy. The surgical methods of induction like stripping of membranes and amniotomy are contraindicated in case of IUFD as it may precipitate infection. While the time-tested method of induction with Oxytocin is painful and less successful as the uterus is less sensitive to oxytocin before term. RCOG in its Green-top Guideline No. 55 recommends a combination of mifepristone and a prostaglandin preparation as the first-line intervention for induction of labour in IUFD which is also endorsed by the NICE guidelines especially for late IUFD.[6,8] Whereas WHO recommends oral or vaginal misoprostol for induction of labour in the third trimester of pregnancy, in women with a dead or anomalous fetus.[9]

As there are two varying schools of thought, this study was undertaken to evaluate and compare the efficacies of both the regimen in an effort to find a better management of woman with IUFD and also to compare the relative advantages and disadvantages of one method over the other.

METHODS

This was a hospital based prospective comparative study taken up in the Department of Obstetrics and Gynaecology, Assam Medical College and Hospital (AMCH), Dibrugarh from 1st July 2015 to 30th June 2016. The study population were pregnant women attending AMCH with diagnosed IUFD. A total number of 90 cases were selected and randomly divided into 2 groups. Approval from Institutional Ethics Committee was taken prior to taking up the study.

The inclusion criteria were women with IUFD at or more than 28 weeks of gestation confirmed with Ultrasound who were not in labour and those who understood the regimen and gave informed written consent.

Exclusion criteria were women who were in labour, cases where vaginal delivery was contraindicated, cases with previous Caesarean deliveries, eclampsia, malpresentation, grand multipara, multiple pregnancy with one intrauterine death, glaucoma, asthma, epilepsy, heart disease, jaundice, renal or hepatic dysfunction and who did not give consent and/or were apprehensive to participate in this study.

A thorough history including patient's demographic features (age, parity, gestational age) was taken and period of gestation was assessed from their Last Menstrual Period (LMP).

Cases were examined thoroughly and all relevant findings were systematically recorded. In all cases, IUFD was confirmed by Ultrasonography and other necessary baseline investigations were done. A written and informed consent was obtained. Cases fulfilling the inclusion criteria were selected and divided into two groups of 45 patients each with first case randomly allocated to Group-A.

The two groups were induced using the following regimen as recommended by RCOG guidelines[8]

- Group A: Single dose of 200mg Mifepristone was given orally. After 24-hours interval, 100 µg of Misoprostol was inserted in the posterior vaginal fornix and repeated every 4 hours till they went into labour or delivered the dead fetus or to a maximum of 6 doses(600µg)
- Group B: 100 µg of Misoprostol was inserted in the posterior vaginal fornix and repeated every 4 hours till they went into labour or delivered the dead fetus, or to a maximum of 6 doses(600µg)

Induction was preferably started early in the morning. Subsequent to misoprostol administration uterine contractions, pulse, blood pressure, temperature and systemic symptoms were monitored 2 hourly and the labour progress was monitored using WHO modified Partograph. In active labour, oxytocin augmentation if required was started after 4 hours of the last dose of misoprostol, using an established standard oxytocin regime of 2 units in one litre 5% dextrose at 15 drops per minute with increments at half hourly intervals.

Successful treatment was defined as delivery within 72 hours of first Misoprostol dose. If the first course of induction was unsuccessful, after a break of 24 hours, second course of induction was started with the vaginal misoprostol of same dose. If not expelled with repeat course, induction was categorized as failed. Labour complications, if any, were managed according to our departmental protocol.

Statistical analysis

Data were analyzed using the SPSS version 17 for Windows Statistical Package. Comparison of numerical variables were done through independent sample t-test and Mann Whitney U test as appropriate. Comparison of categorical variables was done using chi-square test and Fisher Exact test. Variables that were normally distributed were presented as means with standard deviations. Differences were regarded as statistically significant with a p-value <0.05.

RESULTS

Both groups were comparable with respect to socio-demographic characteristics and obstetrical parameters and the comparison is shown in table (Table 1).

Table 1: Socio demographic and obstetrical parameters.

Characteristics	Group A (n = 45)	Group B (n = 45)	p-value
Mean age (yrs)	26.53±4.9	27.13±4.89	0.5624
Mean parity	1.42±1.10	1.11±1.07	0.1788
Mean BMI	23.54±3.45	22.45±3.36	0.1325
Mean gestational age (weeks)	34.47±3.12	34.58±3.31	

Both the groups were found to be comparable with respect to mean Pre – induction Bishops score. The mean Induction to Onset of Labour Interval (i.e. the time interval between first dose of misoprostol and onset of active labour) in Group A was 13.42±4.67 hours and that in Group B was 21.13±10.32 hours. The difference was considered to be extremely statistically significant with a p-value of less than 0.0001. One case in Group A went into active labour with only Mifepristone and hence induction with Misoprostol was not required. Two cases in Group B required a second cycle of Misoprostol and none so in Group A.

Table 2: Comparison of efficacy.

Variable	Group A (n = 45)	Group B (n = 45)	p value
Mean pre-induction Bishops score	3.4±1.54	3.24±1.43	0.6108
Mean induction to onset of labour interval (hours)	13.41±4.67	21.13±10.32	0.0001
Mean induction to delivery interval (hours)	17.43±5.58	25.56±10.78	0.0001
No. of misoprostol doses received	2.76±1.11	4.40±1.46	0.0001
Need for augmentation with oxytocin	7 (15.5%)	12 (26.6%)	0.1965

Induction to delivery interval (the time interval between first dose of Misoprostol to expulsion of the fetus) ranging from 8-28 hours in Group A was compared with induction to delivery interval ranging from 12-72 hours in Group B. Mean Induction to Delivery Interval was 17.43±5.58 hours in Group A which was very less compared to 25.56±10.78 hours in Group B and was statistically found to be extremely significant. Mean dose of Misoprostol required was less in Group A (2.26±1.11) compared to Group B (4.4±1.46) and the difference was statistically considered to be significant with a p-value of 0.0001 since all the cases delivered within 72 hours of start of induction hence the success rate of induction in both the groups were 100%. Out of the 45 cases in Group A only 7 (15.5%) cases required augmentation with oxytocin and of the 45 cases in Group B, 11 (26.6%) cases required augmentation with oxytocin (Table 2).

Table 3: Side effects of inducing agent.

Side effects	Group A (n = 45)		Group B (n = 45)		p value
	n	%	n	%	
Nausea and vomiting	6	13.3	10	22	0.4089
Fever	4	8.8	6	13.3	0.7391
Diarrhoea	2	4.4	0	0	0.4944
Headache	0	0	2	4.4	0.4944
Dizziness	3	6.6	5	11.1	0.7136
Skin rashes	0	0	0	0	-
Excessive pain or cramps	0	0	2	4.4	0.4944
Severe bleeding	0	0	0	0	-
Uterine rupture	0	0	0	0	-

When the side effects of both the inducing agents were compared the tolerance to Group A i.e. Combined regimen was better than Group B i.e. Misoprostol alone regimen. Minor side effects were noted in both the regimens and were comparable (Table 3).

DISCUSSION

Various studies have been conducted in the past to find an ideal method for the induction labour in IUFD. In the present study, statistically significant reduction was observed in the mean Induction to Onset of Labour Interval. Agarwal et al also reported a shorter Induction to Onset of Labour Interval of 9 hours (Range 5-13.5) in the Combination group and 12 hours (Range 5-18.5) in Misoprostol only group, which is comparable to the present study.[14]

In the present study, the mean Induction to Delivery interval for Group A was 17.43±5.58 hrs while it was 25.56±10.78 hrs in group B and the difference was found to be statistically significant. Comparable results were reported by various studies (Vayrynen et al, Sharma et al, Panda S et al, Praveena G et al, Agarwal et al) but the mean interval varies in all the studies.[10-14] The probable reason is difference in the dosage and schedule of Misoprostol used according to various study guidelines.

We found significant decrease in the requirement of Misoprostol with prior use of Mifepristone which is consistent with the literature that shows decreased prostaglandin requirement in cases where Mifepristone was given. In the present study, 15.5% cases in Group A and 26.6% cases in Group B required augmentation with oxytocin. Comparable results were reported by Agarwal

et al with 16% cases in the combination group and 22% cases in Misoprostol alone group requiring oxytocin induction and Panda S et al with no cases in the combination group and 11.3% cases in the Misoprostol alone group requiring oxytocin induction.[12,14]

Delivering an IUFD is a frustrating task for an obstetrician mainly because the uterus is not very receptive to the usual methods of induction before term. Both Mifepristone-Misoprostol Combination Regimen and Misoprostol-alone Regimen have been recommended by different international guidelines for induction of labour in IUFD but till date there is no consensus regarding the ideal regimen.

It was observed in the study that both the regimen was equally safe, easy to administer and affordable but the Combination Regimen had a slight edge over misoprostol alone regimen in terms of tolerance, fewer side effects and efficacy with regard to early onset of labour, shorter Induction to Delivery Interval and relatively less dose of misoprostol than misoprostol alone regimen. Further studies are necessary on a larger population to define the ideal treatment option and optimum dosage for a better management of IUFD.

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